

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-4, 6, and 8-14 are pending and are directed to a library of membrane protein-embedded liposomes (claims 8-11 and 14) and a method of preparing the library (claims 1-4, 6, 12, and 13).

Claims 1-4, 6, 12, and 13 have been labeled as withdrawn, because these claims are directed to a non-elected invention. Since claims 1-4, 6, 12, and 13 depend from the elected claims and are directed to a method of preparing the library of the elected claims, Applicants request that claims 1-4, 6, 12, and 13 be rejoined and considered upon the allowance of claims directed to the elected subject matter.

*Amendments to the Specification*

The specification has been amended to capitalized trademarked terms. In particular, “Polytron” has been replaced with “POLYTRON™.”

The specification also has been amended to correct a typographical error.

No new matter has been added by way of these amendments to the specification.

*Amendments to the Claims*

Claim 1 has been amended to depend from claim 8. In view of the amendment to claim 1, claim 7 has been canceled to prevent redundancy.

Claim 8 has been amended to recite the features of claim 1 and to no longer depend from non-elected claim 1.

Claims 8-10 have been amended to clarify that the amount of membrane proteins is per library, as supported by the specification at, for example, page 25, line 30, through page 26, line 13.

Claim 14 is new and is similar to claim 8, except that claim 14 recites that (i) the library contains  $1 \times 10^6$  or more membrane protein-embedded liposomes, as supported by the

specification at for example, page 25, lines 15-29, and (ii) the weight ratio of membrane proteins to lipids constituting the liposomes is 0.05 or less, as supported by the specification at, for example, page 25, lines 8-17.

Accordingly, no new matter has been added by way of these amendments to the claims.

*Summary of the Office Action*

The Office has maintained the restriction requirement and withdrawn non-elected claims 1-4, 6, 7, 12, and 13 from consideration.

The Office objects to claims 8-11, because claim 8 depends from a non-elected/withdrawn claim.

The Office rejects claims 8-11 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

The Office rejects claims 8-11 under 35 U.S.C. § 103(a) as allegedly unpatentable over Allen et al. (U.S. Patent 6,056,973) and Tanaka et al. (WO 02/056026). The Office also rejects claims 8-11 under 35 U.S.C. § 103(a) as allegedly unpatentable over Perrott et al. (U.S. Patent 6,217,901), Tanaka et al., and Munechika et al. (U.S. Patent 5,662,931).

Reconsideration of these objections and rejections is hereby requested.

*Discussion of the Claim Objection*

The Office objects to claims 8 (and claims 9-11 dependent thereon), because claim 8 depends from a non-elected/withdrawn claim (claim 1). Claim 8, as amended, has been placed in independent claim format and incorporates the features of claim 1.

Applicants believe that the objection to the claims is moot in view of the claim amendments. Therefore, Applicants request that the claim objection be withdrawn.

*Discussion of the Indefiniteness Rejection*

The Office contends that it is unclear in claims 8-10 whether the amount of protein is (i) per liposome or (ii) per library. The pending claims, as amended, recite that the amount of protein is (ii) per library.

Applicants believe that the pending claims, as amended, are sufficiently clear. Therefore, Applicants request that the indefiniteness rejection be withdrawn.

*Discussion of the Obviousness Rejections*

The Office contends that it would have been obvious to one of ordinary skill in the art to make the library of membrane protein-embedded liposomes recited in claims 8-11 based on the teachings of (i) the Allen and Tanaka references and (ii) the Perrott, Tanaka, and Munechika references. The obviousness rejections are traversed for the following reasons.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art “are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned *Graham* factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

As regards the scope and content of the prior art, the Office contends that Allen et al. discloses a library of liposomes comprising proteins, wherein the liposomes are greater than 10 nm in diameter (e.g., 100 nm). The Office acknowledges that Allen et al. does not teach that the library contains 10 fg, 1 pg, 10 pg, or more membrane proteins; however, the Office

contends that Tanaka et al. teaches protein-embedded liposomes comprising ng amounts of protein.

The Office contends that Perrott et al. teaches synthetic polymer complements (SPCs), which are liposomes in a library that range in size from 20-1000 nm. The Office contends that template molecules used to produce the SPCs can be membrane proteins. The Office acknowledges that Perrott et al. does not teach that the library contains 10 fg, 1 pg, 10 pg, or more membrane proteins or a weight ratio of proteins to lipids of 0.01 to 0.8; however, the Office contends that these features are disclosed by Tanaka et al. and Munechika et al., respectively.

For purposes of the analysis here, and for the sake of argument, the level of ordinary skill can be considered to be relatively high, such that a person of ordinary skill in the art would have an advanced degree and/or several years of experience in the relevant field.

The present invention, as defined by the pending claims currently being examined, is directed to a library of membrane protein-embedded liposomes comprising about  $1 \times 10^5$  or more membrane protein-embedded liposomes, which library of membrane protein-embedded liposomes is obtained by (a) providing a library of membrane proteins, and (b) contacting the library of membrane proteins with liposomes to form a library of membrane protein-embedded liposomes, wherein the weight ratio of the membrane proteins to lipids constituting the liposomes is from 0.01 to 0.8, wherein the liposomes have a diameter of 10 nm or more, and wherein the amount of membrane proteins per library is about 10 fg or more.

As set forth in the specification, the number of membrane proteins embedded per liposome, the size of the liposome, and the like (e.g., weight ratio of membrane protein/lipid) influence the properties of the library used for the proteome analysis of membrane proteins (see, e.g., page 8, lines 2-16). None of the cited references, when considered alone or in combination, discloses a library of membrane protein-embedded liposomes with the claimed properties (e.g., the particular weight ratio of membrane protein/lipid).

The Office contends that Allen et al. discloses a liposome formation with 1-20 mole percent of lipid and 1.2 mole percent of protein. Since the molecular weight of lipid

constituting a liposome is about 800, and the average molecular weight of membrane proteins typically is several tens of thousands of Daltons (Da), e.g., 30 kDa, the weight ratio of membrane protein/lipid would be on the order of about 2 to about about 40 or more. In distinct contrast, the particular weight ratio of membrane protein/lipid set forth in the pending claims is 0.01 to 0.8 (claims 8-11) or 0.05 or less (claim 14), i.e., far less than the weight ratio of membrane protein/lipid possibly disclosed in Allen et al.

If anything, the disclosure of Allen et al. teaches away from using the weight ratio of membrane protein/lipid of 0.01 to 0.8, or of 0.05 or less, as recited in the pending claims. Therefore, it would not have been obvious to one of ordinary skill in the art to use a weight ratio of membrane protein/lipid of 0.01 to 0.8, let alone 0.05 or less, based on the disclosure of the Allen and Tanaka references.

The Office acknowledges that Perrott et al. (as well as Tanaka et al.) does not teach a weight ratio of membrane protein/lipid that falls within the claimed range; however, the Office contends that Munechika et al. teaches a weight ratio of protein/lipid of 0.1 to 0.5. Applicants note that Munechika et al. relates to a liposome composition *encapsulating* a protein drug. The proteins exemplified in Munechika et al. are *water-soluble* proteins, such as cytokines and hormones. As such, one of ordinary skill in the art would not have had any reason to combine the disclosure of Munechika et al. with the disclosures of Perrott et al. and Tanaka et al., let alone in the manner necessary to arrive at the inventive library, wherein *membrane* proteins are embedded into the lipid bilayer of the proteoliposome.

For purposes of the analysis here, there is no need to consider any objective criteria of nonobviousness.

Considering all of the *Graham* factors together, it is clear that the present invention – as defined by the pending claims – would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of the cited references. Accordingly, the obviousness rejections should be withdrawn.

*Discussion of the Subject Matter of Claim 14*

The subject matter of claim 14 is entitled to the benefit of the filing date of U.S. Patent Application 10/622,002. Accordingly, claim 14 has an effective U.S. filing date of July 17, 2003.

Tanaka et al. has an earliest possible effective U.S. filing date of January 9, 2001, and was published on July 18, 2002, i.e., within one year of the priority date for claim 14 of July 17, 2003. As a result, Tanaka et al. can only possibly be prior art to claim 14 under Section 102(a) or Section 102(e).

Applicants submit hereweith a Declaration Under 37 C.F.R. § 1.132 from the inventors of the present application. The Rule 132 declaration states that (a) only the inventors listed on the present application conceived of the claimed invention and (b) the remaining individuals listed on Tanaka et al. (i.e., Hiromichi Mukai, Hisashi Arikuni, Mieko Shiwa, and Bungo Ochiai) did not make a contribution to the conception of the invention as defined by the pending claims of the present application. Rather, these other individuals listed on Tanaka et al. were involved in a portion of the invention disclosed in Tanaka et al. that is not being claimed in the present application. Accordingly, Tanaka et al. is not prior art to claim 14 under Section 102(a).

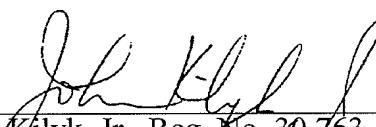
As regards the possibility that Tanaka et al. is prior art to claim 14 under Section 102(e), Applicants note that a patent document that qualifies as prior art under Section 102(e) cannot properly be used to support an obviousness rejection under Section 103(a) if the subject matter of the prior art patent document and the claimed invention of the pending application were commonly owned at the time the invention was made. Mitsubishi Pharma Corporation owned the inventions disclosed and claimed in Tanaka et al. and the inventions disclosed and currently claimed in the present application at the time of invention, as evidenced by (a) the applicant/ownership information reciting Mitsubishi Pharma Corporation as set forth on the face of Tanaka et al. (as well as the assignment of parent U.S. Patent Application 10/038,918 to Mitsubishi Pharma Corporation as recorded by the U.S. Patent and Trademark Office at Reel 013037, Frame 0684, on June 26, 2002), and (b) the assignment of the parent of the present application, namely U.S. Patent Application 10/622,002, to Mitsubishi Pharma Corporation as recorded by the U.S. Patent and Trademark

Office at Reel 014435, Frame 0464, on August 28, 2003 (though Mitsubishi Pharma Corporation subsequently assigned its rights to Protosera Inc.). Accordingly, Tanaka et al. cannot be relied upon as prior art under Section 102(e) against claim 14 for purposes of determining obviousness under Section 103(a).

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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